Amendments to the Specification:

Please delete paragraph 19 and replace it with the following:

[0019] Figure 1 shows the *in vitro* aptamer selection (SELEX) process from pools of random sequence oligonucleotides.

Please delete paragraph 27 and replace it with the following:

[0027] Figure 9 shows a schematic of an agonist SELEX strategy. In this strategy, a target partner (or "TP") or a target partner analog (or "TPA") with agonist-independent affinity for the target is used to screen a diverse molecule library for species which can specifically interact with the TP (or TPA)-target complex. Agonist species may be specifically enriched by (1) selecting against binding to the TP/A, (2) selecting for molecules specifically retained on an immobilized TP/A-target complex, and (3) specifically released from the TP/A-target complex by known high affinity agonists.

Please delete paragraph 28 and replace it with the following:

[0028] Figure 10 shows a schematic of a second agonist SELEX strategy. In this strategy, a target partner or target partner analog is used to screen a diverse molecule library for species which can specifically facilitate formation of the TP (or TPA)-target complex under experimental conditions (*e.g.*, temperature, denaturant, salt concentration, target concentration, or TP/A concentration) such that agonist binding is a prerequisite for target-TP/A complex formation. Agonist species may be specifically enriched by (1) selecting against binding to TP/A and (2) selecting for molecules specifically retained only when the target is added to the immobilized TP (or TPA).

Please delete the text between paragraphs 45 and 46, and replace it with the following:

The SELEX Method

Please delete paragraph 46 and replace it with the following:

[0046] A suitable method for generating an aptamer to gp120 is with the process entitled "Systematic Evolution of Ligands by EXponential Enrichment" ("SELEX") generally depicted in Figure 1. The SELEX process is a method for the *in vitro* evolution of nucleic acid molecules with highly specific binding to target molecules and is described in, *e.g.*, U.S. patent application Ser. No. 07/536,428, filed Jun. 11, 1990, now abandoned, U.S. Pat. No. 5,475,096 entitled "Nucleic Acid Ligands", and U.S. Pat. No. 5,270,163 (see also WO 91/19813) entitled "Nucleic Acid Ligands". Each SELEX-identified nucleic acid ligand is a specific ligand of a given target compound or molecule. The SELEX process is based on the unique insight that nucleic acids have sufficient capacity for forming a variety of two- and three-dimensional structures and sufficient chemical versatility available within their monomers to act as ligands (form specific binding pairs) with virtually any chemical compound, whether monomeric or polymeric. Molecules of any size or composition can serve as targets.

Please delete paragraph 47 and replace it with the following:

[0047] SELEX relies as a starting point upon a large library of single stranded oligonucleotide templates comprising randomized sequences derived from chemical synthesis on a standard DNA synthesizer. In some examples, a population of 100% random oligonucleotides is screened. In others, each oligonucleotide in the population comprises a random sequence and

at least one fixed sequence at its 5' and/or 3' end which comprises a sequence shared by all the molecules of the oligonucleotide population. Fixed sequences include sequences such as hybridization sites for PCR primers, promoter sequences for RNA polymerases (*e.g.*, T3, T4, T7, SP6, and the like), restriction sites, or homopolymeric sequences, such as poly A or poly T tracts, catalytic cores (described further below), sites for selective binding to affinity columns, and other sequences to facilitate cloning and/or sequencing of an oligonucleotide of interest.

Please delete paragraph 50 and replace it with the following:

[0050] Template molecules typically contain fixed 5' and 3' terminal sequences which flank an internal region of 30 – 50 random nucleotides. A standard (1 μmole) scale synthesis will yield $10^{15} - 10^{16}$ individual template molecules, sufficient for most SELEX experiments. The RNA library is generated from this starting library by *in vitro* transcription using recombinant T7 RNA polymerase. This library is then mixed with the target under conditions favorable for binding and subjected to step-wise iterations of binding, partitioning and amplification, using the same general selection scheme, to achieve virtually any desired criterion of binding affinity and selectivity. Starting from a mixture of nucleic acids, preferably comprising a segment of randomized sequence, the SELEX method includes steps of contacting the mixture with the target under conditions favorable for binding, partitioning unbound nucleic acids from those nucleic acids which have bound specifically to target molecules, dissociating the nucleic acid-target complexes, amplifying the nucleic acids dissociated from the nucleic acid-target complexes to yield a ligand-enriched mixture of nucleic acids, then reiterating the steps of binding, partitioning, dissociating and amplifying through as many cycles as desired to yield highly specific high affinity nucleic acid ligands to the target molecule.

Please delete paragraph 53 and replace it with the following:

[0053] In one embodiment of SELEX, the selection process is so efficient at isolating those nucleic acid ligands that bind most strongly to the selected target, that only one cycle of selection and amplification is required. Such an efficient selection may occur, for example, in a chromatographic-type process wherein the ability of nucleic acids to associate with targets bound on a column operates in such a manner that the column is sufficiently able to allow separation and isolation of the highest affinity nucleic acid ligands.

Please delete paragraph 54 and replace it with the following:

[0054] In many cases, it is not necessarily desirable to perform the iterative steps of SELEX until a single nucleic acid ligand is identified. The target-specific nucleic acid ligand solution may include a family of nucleic acid structures or motifs that have a number of conserved sequences and a number of sequences which can be substituted or added without significantly affecting the affinity of the nucleic acid ligands to the target. By terminating the SELEX process prior to completion, it is possible to determine the sequence of a number of members of the nucleic acid ligand solution family.

Please delete paragraph 56 and replace it with the following:

[0056] The core SELEX method has been modified to achieve a number of specific objectives. For example, U.S. Patent No. 5,707,796 describes the use of SELEX in conjunction with gel electrophoresis to select nucleic acid molecules with specific structural characteristics, such as bent DNA. U.S. Patent No. 5,763,177 describes SELEX based methods for selecting

nucleic acid ligands containing photoreactive groups capable of binding and/or photocrosslinking to and/or photoinactivating a target molecule. U.S. Patent No. 5,567,588 and U.S. Application No. 08/792,075, filed January 31, 1997, entitled "Flow Cell SELEX", describe SELEX based methods which achieve highly efficient partitioning between oligonucleotides having high and low affinity for a target molecule. U.S. Patent No. 5,496,938 describes methods for obtaining improved nucleic acid ligands after the SELEX process has been performed. U.S. Patent No. 5,705,337 describes methods for covalently linking a ligand to its target.

Please delete paragraph 57 and replace it with the following:

[0057] SELEX can also be used to obtain nucleic acid ligands that bind to more than one site on the target molecule, and to obtain nucleic acid ligands that include non-nucleic acid species that bind to specific sites on the target. SELEX provides means for isolating and identifying nucleic acid ligands which bind to any envisionable target, including large and small biomolecules including proteins (including both nucleic acid-binding proteins and proteins not known to bind nucleic acids as part of their biological function) cofactors and other small molecules. For example, see U.S. Patent No. 5,580,737 which discloses nucleic acid sequences identified through SELEX which are capable of binding with high affinity to caffeine and the closely related analog, theophylline.

Please delete paragraph 58 and replace it with the following:

[0058] Counter- SELEX is a method for improving the specificity of nucleic acid ligands to a target molecule by eliminating nucleic acid ligand sequences with cross-reactivity to one or more non-target molecules. Counter- SELEX is comprised of the steps of a) preparing a

candidate mixture of nucleic acids; b) contacting the candidate mixture with the target, wherein nucleic acids having an increased affinity to the target relative to the candidate mixture may be partitioned from the remainder of the candidate mixture; c) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture; d) contacting the increased affinity nucleic acids with one or more non-target molecules such that nucleic acid ligands with specific affinity for the non-target molecule(s) are removed; and e) amplifying the nucleic acids with specific affinity to the target molecule to yield a mixture of nucleic acids enriched for nucleic acid sequences with a relatively higher affinity and specificity for binding to the target molecule.

Please delete the Abstract and replace it with the following:

Methods are provided for identifying aptamer regulators. Aptamer regulators are aptamers that bind to a target wherein binding of the aptamer regulator to the target increases the binding affinity of the target for a target partner relative to the affinity of the target for the target partner when the target is not bound by the aptamer regulator such that binding of the aptamer regulator to the target is a prerequisite for target-target partner complex formation.